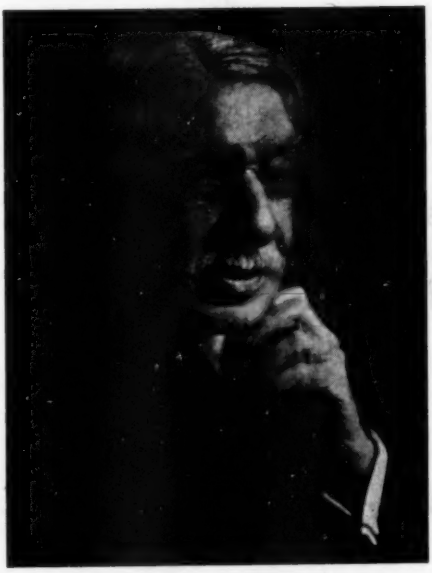
PERIODICAL

PUBLIC LIBRARY
DETROIT

American Journal of Pharmacy

AND THE SCIENCES SUPPORTING PUBLIC HEALTH



DR. SOLOMON SOLIS-COHEN
1857-1948
Eminent Physician, Educator
and Humanitarian

Since 1825 *August 1948*

Pharmacy - - Chemistry
Bacteriology - - Biology

FOUNDED
1821

Undergraduate curricula in these four fields, lead to B. Sc. degrees. Selected graduate studies also available. Co-educational. Applications now being considered for future entering classes. Write for catalog.

Philadelphia College of Pharmacy and Science

43d St., Woodland and Kingsessing Aves.
Philadelphia 4, Pa.

American Journal of Pharmacy

Published monthly by the Philadelphia College of Pharmacy and Science
43d Street, Kingsessing and Woodland Avenues, Philadelphia 4, Pa.

Annual Subscription, $3.00 — Foreign Postage, 25 Cents Extra
Single Numbers, 30 Cents — Back Numbers, 50 Cents

Entered as Second-Class Matter March 27, 1937, at the Post Office at Philadelphia, Pa.
Under Act of March 3, 1879

ever-widening demand

for PROLUTON

(*progesterone*)

"hormone of pregnancy"

IN PURE FORM

Physicians have been quick to see the exceptional merit of PROLUTON* (corpus luteum hormone) by injection. PROLUTON (progesterone) offers physiologically sound medication in many stubborn gynecologic conditions, for its use constitutes replacement of nature's own deficiency. As PROLUTON is the pure, crystalline corpus luteum hormone, its potency is high and unvarying.

naturally EFFECTIVE

Because its action is similar to that of the progestational hormone of the mammalian ovary, PROLUTON is remarkably successful in correcting disorders characterized by deficiency of corpus luteum hormone. Virtually a specific in controlling abnormal uterine motility, PROLUTON has proved of major worth in forestalling such a catastrophe as abortion and in controlling functional uterine hemorrhage. It is likewise of value in relieving painful menstruation, without the need for sedation.

Physicians using PROLUTON have learned to place full confidence in it, for even in high dosage, it has no disturbing side effects.

PACKAGING: PROLUTON (progesterone in oil) ampuls of 1 cc. containing 1, 2, 5 or 10 mg.; boxes of 3, 6 and 50 ampuls; also vials of 10 cc. containing 25 mg. per cc.; box of 1 vial. PRANONE* (anhydrohydroxy-progesterone) tablets of 5 or 10 mg.; boxes of 20, 40, 100 and 250 tablets, and 25 mg.; boxes of 20 and 100 tablets.

*℞

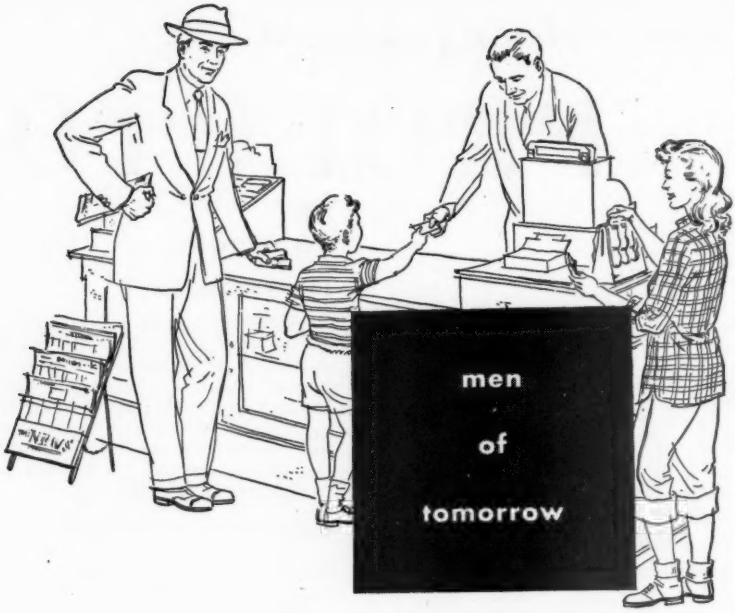
IN PREFERRED POSITION

SCHERING

Schering CORPORATION

BLOOMFIELD, NEW JERSEY

IN CANADA, SCHERING CORPORATION LIMITED, MONTREAL



Nothing is more important to the pharmacist of today than the men and women of tomorrow. The little people who come to the pharmacy on simple errands are the fathers and mothers of a generation to come. The bright face of a child is a challenge to deserve the confidence so freely imposed. Diligent attention to the needs of the young is a professional responsibility. Eli Lilly and Company today is privileged to serve countless physicians and pharmacists whom it served indirectly as children five, six, or seven decades ago. Through the years it has sought to deserve the confidence of the physician, who prescribes, and the pharmacist, who dispenses, by making sincere, honest contribution to both public service and medical care.

ELI LILLY AND COMPANY

WE PAY HIM BUT HE WORKS FOR YOU

INDIANAPOLIS 6, INDIANA, U.S.A.

AMERICAN JOURNAL OF PHARMACY

AND THE SCIENCES SUPPORTING PUBLIC HEALTH

Since 1825

LINWOOD F. TICE, Ph. G., B. Sc., M. Sc., Editor

Kenneth Avis, M. Sc., and Charles F. Sharpe, M. Ed., Editorial Assistants

John E. Kramer, B. Sc., Business Manager

COMMITTEE ON PUBLICATION

E. Fullerton Cook, P. D., Ph. M., M. S., Chairman

Mitchell Bernstein, P. D., F. A. C. P.

Marin S. Dunn, A. M., Ph. D.

Louis Gershenfeld, P.D., Ph.M., D.Sc.

J. W. Sturmer, Phar. D., Ph. M., D. Sc., Secretary

Ivor Griffith, P. D., Ph. M., D. Sc., F. R. S. A., ex officio

Vol. 120 AUGUST 1948 No. 8

CONTENTS

In Memoriam:

Dr. Solomon Solis-Cohen 274

Editorial:

The "Inert" Glandulars 276

Articles:

The Bactericidal Efficiency of Crude Iodine in (0.1 N) Alkali. By L. Gershenfeld and D. Fox 279

Specifications for a Good Antigen As Seen by the Pediatrician. By F. H. Top 287

The Pharmaceutical Survey—The Beginnings of the End. By E. C. Elliot 293

Selected Abstracts 305

Book Reviews 312

IN MEMORIAM

DR. SOLOMON SOLIS-COHEN

1857-1948.

DR. SOLOMON SOLIS-COHEN of Philadelphia, eminent diagnostician, distinguished therapeutist, noted author, scholar, and poet, died on July 12, 1948 in the Jewish Hospital, Philadelphia, Pennsylvania, at the age of 90.

Dr. Solis-Cohen was born in Philadelphia in 1857. He was graduated from Central High School before he was 16 and received his medical degree from the Jefferson Medical College in 1883. Entering the practice of medicine, he joined the faculty of the Jefferson Medical College in 1884 and in 1902 was made professor of clinical medicine. Upon his retirement from the faculty in 1927, he was named professor emeritus. From 1897 to 1902 he taught at the Philadelphia Polyclinic; from 1890 to 1892 he lectured on therapeutics at Dartmouth. In 1903 he was chairman of the therapeutic section of the American Medical Association. From 1887 to 1927 he was physician to the Philadelphia General, Jewish, and Jefferson Hospitals of Philadelphia.

Dr. Solis-Cohen was president of the Philadelphia County Medical Society in 1898 and 1899; he was recorder of the Association of American Physicians from 1899 to 1913. He was a Fellow of the American College of Physicians and the Philadelphia College of Physicians.

A member of the Philadelphia Board of Education from 1925 to 1944, Dr. Solis-Cohen was deeply interested and participated in civic, national, and international affairs.

Dr. Solis-Cohen was editor of the *Polyclinic* from 1894 to 1899 and *American Medicine* from 1901 to 1905. He edited *A System of Physiologic Therapeutics* in 1902. He published *Essentials in Diagnosis* in 1892 in collaboration with A. A. Eshner and a textbook, *Pharmacotherapeutics, Materia Medica and Drug Action* in 1928 with Thomas S. Githens.

In 1894 Dr. Solis-Cohen published in the *American Journal of Medical Science* the first comprehensive study on vasomotor-ataxia and the relationship of various disorders including what later were

termed allergic phenomena and sympathicotonia and vagotonia and currently termed autonomic imbalance. In addition, Dr. Solis-Cohen wrote a host of scientific papers on varied medical subjects.

Dr. Solis-Cohen was a devoted friend of many pharmacists and a staunch supporter of the science of pharmacy. In 1890, Dr. Solis-Cohen's paper on the standardization of galenical preparations was well received. His many notes and editorials on nostrums in various journals and his stand against patent medicine quackery remain monumental. The 1892 Alumni Report of the Philadelphia College of Pharmacy and Science contains his paper on the attitude of the medical profession towards the nostrum traffic.

He addressed the Philadelphia Branch of the American Pharmaceutical Association on "The Function of the True Pharmacist" in 1906, and the Philadelphia County Medical Society and the Philadelphia Branch of the American Pharmaceutical Association on "Where Shall the Pharmacopeia Draw the Line of Demarcation" in 1910. Other outstanding papers on pharmaceutical subjects include "Prescribing of Proprietaries, Especially Proprietary Mixtures," "The Pharmacopoeia: What It Is and What It Is Not." He addressed the 59th and 64th Annual Meetings of the American Pharmaceutical Association, and spoke on June 14, 1921 at the celebration of the first century of the Philadelphia College of Pharmacy in Philadelphia. These addresses can be read with profit to-day.

Dr. Solis-Cohen was a member of the Committee of Revision of the U. S. Pharmacopoeia, 1910 to 1920, and chairman of the Scope Subcommittee. He was a member of the Board of Trustees of the U. S. Pharmacopoeia from 1920 to 1940.

Living at the time when therapeutic nihilism was taught by many prominent medical authorities, Dr. Solis-Cohen was a great advocate of the use of drugs as therapeutic agents. His dictum, "The right drug at the right time in the right dose will do the right thing" will long be remembered by his many medical students.

Genial in manner, kindly in spirit, ever-ready with a helping hand to his colleagues, particularly the young physician, Dr. Solis-Cohen was an inspiration to all of those who had the good fortune of knowing him. Of his death it can be truly said that the world has suffered an irreparable loss.

MITCHELL BERNSTEIN, M. D.

EDITORIAL

THE "INERT" GLANDULARS.

THE action of the Food and Drug Administration relative to the inert glandular drugs is one which deserves careful thought. On the technical ground that these drugs cannot be demonstrated to contain any active constituents and that therefore they cannot be adequately labeled, the F. D. A. plans to ban them from interstate commerce and proscribe their use. The claim has been made that these drugs are used by the physician solely by reason of the demand created by the manufacturers' advertising. This we doubt.

It would be difficult indeed to refute the argument that such substances as dried and defatted ovary, orchic substance, anterior pituitary, and the like, possess no demonstrable endocrine action when tested on animals. Only thyroid when administered orally is recognized to exert an endocrine effect, although posterior pituitary has some action when administered by nasal insufflation.

We can see no objection to some action by the F. D. A. in bringing this to the attention of the medical and pharmaceutical professions, if it wishes. This has already been done by a number of groups including the Council on Pharmacy and Chemistry of the American Medical Association. Our objection lies in the bureaucratic and dictatorial flavor of an action which presumes to tell *bona fide* physicians that they are no longer free to prescribe a drug which they have used for a decade or longer and which they may still wish to prescribe. Surely this is governmental interference in what has always been the prerogative of the physician. We have no argument against the new drug regulations of the F. D. A. nor against actions which regulate the use of dangerous drugs, but drugs so old and harmless as these glandulars can hardly be classified as new or dangerous. Can it be that the F. D. A. considers the medical profession so lacking in judgment that some of the drugs that many of its practitioners consider useful must be taken from them by government action?

Another objectionable feature of this action is that the F. D. A. now in effect supersedes the National Formulary Committee in the

matter of the scope of the N. F. One of the real examples of democracy in action in the United States has been the procedure followed in the issuance of the official books, the United States Pharmacopoeia and the National Formulary. True it is that use dictates the scope of the N. F., but by thus banning the use of a glandular its official recognition is automatically cancelled in the next edition. Organized pharmacy would do well to consider the possible future implications of such action should this present radical step be allowed to go unchallenged.

We do not for a moment question the integrity of the F. D. A., but it would appear that in its honest efforts to protect the public it has been somewhat over-zealous, so much so that a stand has been taken that cannot be supported if all the facts are considered. Scientists, generally, are likely to make the mistake of judging an issue only from the viewpoint of their own field of specialization. The pharmacologist who is expert at evaluating the physiologic effect of a drug on a test animal, like the rat, is almost certain to overlook the fact that the practice of medicine is not just a simple projection of his results. The treatment of human patients involves a number of conditions and factors not capable of being duplicated or evaluated by animal experimentation. Let us, for example, set up a hypothetical case which many wise physicians might conceivably cite from their records. A woman at menopause visits her physician and consultation shows that she is emotionally disturbed by purely psychosomatic factors. Knowing that she is reaching the end of her procreative life, she has a hidden fear that she may lose her appeal for her husband and is concerned over the possible competition that she may face. Careful study convinces the physician that no real need exists for potent estrogens so he gives reassuring advice and, in order to help the patient mentally and thus physically, he prescribes capsules containing powdered ovary. The patient knowing that she is taking powdered ovary, for it can be read on the prescription, has new confidence and self-assurance for subconsciously she feels that her "lack" is being taken care of. Can one deny, in the face of the marked subjective improvement that takes place, the value of this drug? Is it not a far wiser thing to give an "inert" drug where no potent estrogen is needed than to give no drug at all or else be forced to give one of the estrogens? The narrow-minded scientist might say, " 'Tommyrot,' if the patent needs

no therapy, tell her so." But can human beings be handled like test tubes, balances and white mice?

The greatest problem facing civilization today is the fact that we have concentrated on training scientific specialists who have super minds but in one direction only. Thus we have some physicists, chemists, mathematicians and so-forth who in other ordinary walks of life are not as well versed or adapted as little children. They create and have created monsters with no thought or concern over their social effects and consequences. So much have we worshipped pure science that many have come to believe it the one and only goal of mankind with human happiness of little consequence.

It would be well for those in positions where decisions are made, to realize and recognize that the sharp lines of demarcation between good and bad, active and inert, true and false are seen sharply only by one whose vision is limited. In matters affecting others and human affairs, it is rarely possible for the scientist to trust his own narrow viewpoint if he wishes to act wisely and for the common good. It is extremely doubtful that the action of the F. D. A. on glandulars would stand the test of any unbiased jury were all the facts concerning this problem made known. If they are to be deleted from the practice of medicine, let it be done by the slow orderly process of education and not by dramatic action based on the results of the experimental pharmacologist, valid though they may be.

L. F. Tice.

THE BACTERICIDAL EFFICIENCY OF CRUDE IODINE IN (0.1 N) ALKALI

By Louis Gershenfeld and David Fox *

History

THE antiseptic action of iodine was first discovered in 1873 by C. J. Davaine (1). From this period on, considerable literature has appeared on the use of this antiseptic as a skin sterilizing agent. Later, Vergnoux (2) experimented with the possibility of the use of Iodine Tincture for the rapid sterilization of water supplies. This was the first article to appear on the use of iodine as a sterilizing agent for drinking water. Two years later, Bachman (3) reported that the addition of three to six drops of Tincture of Iodine to each quart of water served as a bactericidal agent for disease-producing bacteria. The following year, Hinman (4) also discussed the importance of water purification with iodine.

In 1933, Beckwith and Moser (5) compared the efficiencies of all the halogens as germicides. Studies were conducted upon the killing effects on large inocula of bacteria derived from soil suspensions and likewise upon water to which were added cultures of *E. coli.* They reported that the activity of each of the halogens upon that portion of water derived from soil suspensions was approximately equal. Additions of as little as 0.1 p. p. m. of each indicated marked lethal efficiencies. When the comparative germicidal values of chlorine, bromine, and iodine upon *E. coli* were considered by them, each was found to reveal high potency. Four years later, in 1937, Pond and Willard (6) reported that two drops per liter of 7% Tincture of Iodine made drinking water safe for human consumption in fifteen minutes.

Nyiri and Dubois (7) noted that when iodine acts as a disinfectant, elemental iodine is the effective agent, and that the iodine in the molecular structure is too firmly bound to be effective.

* Department of Bacteriology, Philadelphia College of Pharmacy and Science.

Most iodine solutions and tinctures employed as bactericidal agents contain soluble iodides. The only data found in the literature pertaining to bactericidal iodine solutions not containing a soluble iodide was that reported by Chandler and Miller (8). These workers presented a stable suspensoid of iodine that contained neither iodides nor alcohol. This was prepared by acidification at 0° C. of sodium iodohypoiodite containing acacia as a protective colloid.

Purpose

In order to use aqueous solutions containing iodine as disinfectants, a soluble iodide, usually sodium or potassium, is added to

TABLE I

PHENOL COEFFICIENT OF CRUDE IODINE IN 0.1 N ALKALI

pH	Temp.	5 cc. quantities of Iodine Dilution	0.5 cc. Salmonella (E.) typhosa 5 min. contact	10 min. contact	15 min. contact	Phenol Coefficient
9.55	20.5° C.					5.06
		1:353	0	0	+	
		1:412	0	0	+	
		1:470	+	+	+	
		1:530	+	+	+	
	Control	Phenol Dilution				
		1:80	0	0	0	
		1:90	+	+	0	
		1:100	+	+	+	
8.32	19° C.	Iodine Dilution				6.59
		1:470	0	0	0	
		1:530	0	0	0	
		1:590	+	+	0	
		1:647	+	+	+	
	Control	Phenol Dilution				
		1:80	+	0	0	
		1:90	+	0	0	
		1:100	+	+	0	
		1:110	+	+	+	

dissolve the free iodine. Economically, the addition of the iodide increases the cost of disinfection. Therefore, the problem was the preparation of a free iodine disinfecting solution which could be used for inanimate objects, in swimming pools, and which would not require either sodium iodide or potassium iodide and thus be cheaper in cost.

Experimental

It was found that iodine was soluble in a weak alkali solution. The solubility of crude iodine * in 0.1 normal sodium hydroxide solution was determined. The bactericidal efficiency of such an iodine solution at varying degrees of pH was determined. The procedure used was a modified phenol coefficient technique** (9).

The solubility of crude iodine in 0.1 normal sodium hydroxide was determined as follows: Crude iodine was added to the 0.1 normal hydroxide solution until saturated and permitted to stand for thirty minutes with occasional stirring. One hundred cubic centimeters of the supernatant fluid were removed at the end of this period and the iodine content determined by acidifying the solution with 4 normal sulfuric acid and then titrating with sodium thiosulfate using starch indicator (11). The Hopkins strain of *S. typhosa* (9) was the test organism employed in the bactericidal efficiency tests. A stock culture of the organism was kept on F. D. A. agar. Daily transplants of the organism were made in F. D. A. bouillon. Fresh transplants from the stock culture were made every three weeks.

A modified F. D. A. phenol coefficient test was performed. The hydrogen ion concentration of the disinfecting solution was varied, and the bactericidal effect was noted at each pH. A range of pH values varying from 9.55, 8.32, 7.62, 7.08, 6.53, 5.36, to 4.93 was obtained by the use of Clark and Lub's buffer system (potassium monohydrogen phosphate and sodium hydroxide) (10). It was necessary to employ phosphoric acid to obtain pH values below seven. The temperatures at which the tests were carried out varied from 19° to 22.5° C.

An attempt to determine the parts per million of free iodine in the iodine solution at the pH range was made spectrophotometrically

* The iodine used in this study was crude Chilean iodine.

** Difco's Extract was substituted for Liebig's Beef Extract.

using alpha-naphthaflavone indicator. Because of the formation of a precipitate upon the addition of the iodine solution to the indicator, this could not be accomplished. Using a 1:10,000 iodine solution and phosphate and acetate buffer solutions in a 1:1 ratio, the authors determined the time for precipitation to occur in the pH range of 6.6 to 7.8.

Findings

The solubility of the crude iodine in 0.1 normal sodium hydroxide was 1.694% of iodine.

In a temperature range of 19° to 22.5° C., it was observed that 1.694% of total iodine added in 0.1 normal sodium hydroxide solu-

TABLE II

PHENOL COEFFICIENT OF CRUDE IODINE IN 0.1 N ALKALI

pH	Temp.	5 cc. quantities of Iodine Dilution	0.5 cc. Salmonella (E.) typhosa 5 min. contact	10 min. contact	15 min. contact	Phenol Coefficient
7.62	20° C.					7.00
		1:470	0	0	0	
		1:530	0	0	0	
		1:590	+	+	+	
		1:647	+	+	+	
	Control	Phenol Dilution				
		1:80	+	0	0	
		1:90	+	+	+	
		1:100	+	+	+	
7.08	20° C.	Iodine Dilution				7.75
		1:530	0	0	0	
		1:590	0	0	0	
		1:647	0	+	+	
		1:706	+	+	+	
	Control	Phenol Dilution				
		1:80	+	0	0	
		1:90	+	+	+	
		1:100	+	+	+	

tion showed phenol coefficients of 5.06, 6.59, 7.00, 7.75, 10.6, 11.76, 17.58, and 20.24 at the respective pH values of 9.55, 8.32, 7.62, 7.08, 6.53, 6.07, 5.36, and 4.93.

In the pH range of 6.6 to 7.8, it was observed that the phosphate buffered solution of 1:10,000 free iodine when added to alpha naphthaflavone indicator took 40 to 50 sec., 50 to 60 sec., 45 to 50 sec., 80 to 90 sec., 50 to 60 sec., 45 to 50 sec., and 40 to 50 sec. for the formation of a precipitate at the respective pH of 6.6, 6.8, 7.0, 7.28, 7.4, 7.6, and 7.85. With the acetate buffered solution, it required 35 to 45 sec., 30 to 40 sec., 25 to 30 sec, 30 to 40 sec., 60 to 70 sec., 55 to 60 sec., and 40 to 50 sec. for precipitation to occur at the respective pH of 6.6, 6.8, 7.0, 7.2, 7.4, 7.6, and 7.8.

TABLE III

PHENOL COEFFICIENT OF CRUDE IODINE IN 0.1 N ALKALI

pH	Temp.	5 cc. quantities of Iodine Dilution	0.5 cc. Salmonella (E.) typhosa 5 min. contact	10 min. contact	15 min. contact	Phenol Coefficient
6.53	21° C.					10.6
		1:706	0	0	+	
		1:765	0	0	0	
		1:823	+	+	+	
	Control	Phenol Dilution				
		1:70	0	0	0	
		1:80	+	+	0	
		1:90	+	+	0	
		1:100	+	+	+	
6.07	20.5° C.	Iodine Dilution				11.76
		1:941	0	0	0	
		1:1059	0	0	0	
		1:1176	0	+	+	
		1:1294	0	+	+	
	Control	Phenol Dilution				
		1:80	0	0	0	
		1:90	0	+	0	
		1:100	+	+	+	

Tables I to IV record the results of the phenol coefficient tests. The buffer with the addition of phosphoric acid showed no bactericidal effect when it was employed as a control.

Discussion

The bactericidal efficiency of iodine solutions depending upon elemental iodine, the increase in the amount of free iodine within the solution was indicated by an increase in the phenol coefficient. In an alkaline solution, the reaction between iodine and sodium hydroxide may form sodium iodide, sodium hypoiodite, or sodium iodate.

$$I_2 + 2NaOH \rightarrow NaI + NaIO + H_2O$$
$$3I_2 + 6NaOH \rightarrow 5NaI + NaIO_3 + 3H_2O$$

TABLE IV

PHENOL COEFFICIENT OF CRUDE IODINE IN 0.1 N ALKALI

pH	Temp.	5 cc. quantities of Iodine Dilution	0.5 cc. Salmonella (E.) typhosa 5 min. contact	10 min. contact	15 min. contact	Phenol Coefficient
5.36	21 °C.					17.58
		1:1412	0	0	0	
		1:1529	0	0	+	
		1:1647	0	+	+	
		1:1765	0	+	+	
	Control	Phenol Dilution	0	0	0	
		1:80				
		1:90	+	0	0	
		1:100	+	+	+	
4.93	22.5° C.	Iodine Dilution				20.24
		1:1647	0	0	0	
		1:1765	0	0	0	
		1:1882	+	+	+	
	Control	Phenol Dilution				
		1:80	0	0	0	
		1:90	+	0	0	
		1:100	+	+	+	
		1:110	+	+	+	

As the alkalinity is decreased or acidity increased, more elemental iodine is liberated. The starting point of this liberation of free iodine is unknown, although it occurs at an alkaline pH. In acid solution, the reaction forms more free iodine.

$$NaI + NaIO + H_2SO_4 \rightarrow I_2 + Na_2SO_4 + H_2O$$
$$5NaI + NaIO_3 + 3H_2SO_4 \rightarrow 3I_2 + 3Na_2SO_4 + 3H_2O$$

The pH values used in the experiments were kept within a range which theoretically gave no germicidal effect *per se* because of alkalinity (sodium hydroxide) or acidity (phosphoric acid). The buffer solutions used to keep the pH values constant did not act as a bactericide.

Conclusions and Summary

The solubility of crude iodine in 0.1 normal sodium hydroxide was found to be 1.694% of iodine.

More free iodine was liberated as the pH became more acid. The free iodine acted as a bactericidal agent and the phenol coefficient was increased.

The phenol coefficient (Salmonella (*E.*) *typhosa*) varied from 5 at pH 9.55 to 20 at pH 4.93, the temperature approximating 20° C. For a summary of the tests see Table V.

The phosphoric acid solution added to the buffer system showed no bactericidal effect.

TABLE V

SOLUTION OF 1.694% CRUDE IODINE IN 0.1 N NaOH

pH	Phenol Coefficient	Temperature
9.55	5.06	20.5° C.
8.32	6.59	19° C.
7.62	7.00	20° C.
7.08	7.75	20° C.
6.53	10.6	21° C.
6.07	11.76	20.5° C.
5.36	17.58	21° C.
4.93	20.24	22.5° C.

BIBLIOGRAPHY

(1) Gershenfeld, Louis, and Miller, Ruth E.: *J. Am. Pharm. Assoc., 21*:894 (1932).

(2) Vergnoux: *Chemical Abstracts, 9*:2954 (1915).

(3) Bachman, F.: *Abstracts of Bacteriology, 1*:326 (1917).

(4) Hinman, J. J.: *Univ. of Iowa Monographs, Studies in Medicine* (August, 1918).

(5) Beckwith, T. D., and Moser, J. R.: *J. Am. Water Works Assoc., 25*:367-74 (1933).

(6) Pond, M. A., and Willard, W. P.: *J. Am. Water Works Assoc., 29*:1995-98 (1937).

(7) Nyiri, Wm., and Dubois, Louis: *J. Am. Pharm. Assoc., 20*:6 (1931).

(8) Chandler, W. L., and Miller, E. J.: *J. Physical Chemistry, 7*:31 (1927).

(9) Circular 198, Food and Drug Administration, United States Department of Agriculture (December, 1931).

(10) Britton: *Hydrogen Ions, Applied Chemistry*, vol. 3 (1929). Van Nostrand, N. Y.

(11) Kolthoff and Sandell: *Quantitative Inorganic Analysis* (1943). Macmillan Co., N. Y.

SPECIFICATIONS FOR A GOOD ANTIGEN AS SEEN BY THE PEDIATRICIAN*

By Franklin H. Top, M. D., M. P. H., F. A. C. P.**

PROTECTION against infectious diseases is gained by virtue of reaction of body cells to bacterial substances called antigens. Recovery from naturally acquired disease is the result of such action, but protection thus obtained is oftentimes purchased at great cost in severe illness with the risk of death. Shortly after the bacteriological era was ushered in, it was found that inoculation of animals and man by use of antigens was in many instances a good substitute for attaining protection by natural means without the risk involved in the latter. As a consequence, tremendous strides have been made in producing protection in man by artificial means; that is, by inoculation of an antigen specific for a disease. The attainment of our present-day status in the prevention of disease by inoculation has not been without its stormy episodes. The struggle for ever better antigens continues.

One of the most potent weapons against infectious disease from the preventive standpoint is active immunization. Unfortunately, this is true for only certain diseases. In the battle against diseases preventable by inoculation, many forces have been allied, including biologists, manufacturers of biologicals and the medical profession, among others. Because their practice is limited to children, pediatricians have been in the vanguard among medical groups with relation to prevention of disease by active immunization, for primary inoculation against childhood diseases begins in infancy. The pediatrician is actually a general practitioner to childen and as such keeps a maintained interest in the children committed to his care, which extends into early adulthood. It is his duty not only to minister to the sick child but it is his larger duty today, insofar as he can, to prevent children from becoming sick. In active immunization against

* Presented before the American Drug Manufacturers' Association Convention, June, 1948.

** Director, Herman Kiefer Hospital, Detroit, Michigan, and Clinical Professor of Preventive Medicine and Public Health, Wayne University College of Medicine, Detroit, Michigan.

certain infectious diseases he has a potent weapon in his armamentarium. His interest lies not only in using antigens of proven worth, but knowing the deficiency of even time honored antigenic agents, eagerly looks for improvements in them. The desirability of protection against other infectious diseases keeps him alert for the discovery of a new antigen, and he is likely to be one of the first among medical men to use it.

The pediatrician is or should be a near perfectionist with relation to the use of antigens in the prevention of disease, for his unit is the individual in contrast to the health officer whose unit is the community or mass of individuals. And because he deals with the unit—a patient—he desires protection for every one of his patients. The pediatrician is looking for an antigen that incorporates the greatest protection available with the least amount of reaction and one which can be administered readily, easily and painlessly and is within the monetary reach of all his patients. How can he most closely approximate this goal and what should be his attitude toward the well nigh multitudinous products, old and new, which beckon him to their use when he is usually neither qualified by training nor scientific exactitude to measure their attributes and inoculates an insufficient number of children to measure their differences. He must, to a large extent, depend upon the scientific qualifications of the biological research staffs of the firms who manufacture the antigens he uses and upon the integrity and reliability of these firms. Secondly, he depends upon an organization who sets standards for quality, purity and uniformity of a product. In the United States, antigenic products must be produced by reputable biological or pharmaceutical firms and must meet the rigid standards set up by the National Institute of Health. Happily, this is so, because in the past, without such provision, serious accidents have happened which in the final analysis harmed the cause of active immunization immensely. In fact, under the most careful scrutiny accidents may happen, and any safeguards against such occurrences which are reasonable to carry out should by all means be instituted. In this respect it is reassuring to note the earnest desire and willingness of reputable firms to initiate safeguards and to welcome industry-wide controls.

Granted there are many acceptable and safe products available for active immunization against a number of diseases, why is it that

pediatricians and other practitioners of medicine as well, inoculate against so few diseases? The approval of a reputable firm's antigen by the National Institute of Health does not assure the popularity of a product. What decides the popularity of a product? Answers to the above questions may be found, at least in part, in the criteria which pediatricians unconsciously apply to an antigen. What are the specifications for a good antigen as seen by the pediatrician? The specifications are likely to be effectiveness, safety, usefulness, ease of administration, and lastly, cost; perhaps there are others. All of the specifications mentioned are interdependent, for if one is not satisfactorily met, an antigen is not likely to be widely accepted. It would be foolish to inoculate a child with a safe but non-effective or useless product, or to give a safe and effective antigen which was difficult to administer, or not useful, or the cost of which was prohibitive. It is somewhat difficult to evaluate the relative importance of the above-mentioned specifications, and their order in this discussion is arbitrary. From the practical standpoint the pediatrician is primarily interested in complete protection and hence efficacy would likely rate first choice with him. However, both safety and cost are very practical considerations.

Effectiveness

An antigen should be capable in the human of producing a degree of protection comparable to that furnished by a natural attack of the disease. The pediatrician would like a high degree of protection in every child inoculated. Unfortunately this is not possible, as cumulative experience with antigenic stimulation has demonstrated. Adequate assessment of a product is difficult, but successes and failures will be noted in practice and in conference with others, or by keeping abreast of developments in the field. Through reading and attending meetings, the pediatrician will gain an impression concerning effectiveness which will either invite him to use or deter him in the use of an antigen. In addition, his attitude will be modified by whether the disease in question is generally mild or usually severe, for in the latter instance even partial protection would likely reduce severity of the infection and risk of death. But in either case there is little need for an antigen that gives a poor degree of protection.

Pediatricians have learned the value of maintaining protection against disease by the utilization of reinforcing or "booster" doses of antigen. At best, protection produced by specific antigens is relatively short-lived, for protection against infectious diseases, where afforded, is dependent upon frequent restimulation whether this be natural or artificial. When natural restimulation against an infection like diphtheria lags because of a low incidence of cases and carriers, the need for more frequent artificial stimulation is greater; hence, the administration of "booster" doses of diphtheria toxoid at intervals after primary inoculation, particularly under the age of ten years.

Safety

No matter how effective an antigen may be the danger attendant upon its administration should be much less than the hazard of the disease it protects against. In the not too distant past, when antigens were in a much less purified state than now obtains, reactions were too often more serious than an attack of the disease. Fortunately, antigens now contain less foreign protein then heretofore and are constantly being improved with relation to this factor, so that the likelihood of severe reactions or death is minimized. Reactions have not been and should not be deterrents to the use of antigens if the disease for which protection is sought is severe. Smallpox vaccination has usually been attended by some reaction both local and general and yet pediatricians are staunch advocates of its use, for the disease they protect against is a severe one. However, a disease like measles or chickenpox with a low hazard to life would necessitate an antigenic agent with but slight risk of severe reactions. An antigen has long been sought for protection against poliomyelitis but first experience with two types in humans slightly more than thirteen years ago was very discouraging and was the cause of a number of unfortunate reactions. Work on this problem is continuing, but any antigen for prevention of poliomyelitis will have to be exceedingly safe, for the attack rate of the disease in severe epidemics rarely exceeds three per thousand of the population. Thus, if protection against the disease were obtained in all inoculated persons, it would spare only three cases per thousand protected, and of these roughly one-half would show weakness or paralysis. The chance of death during such an epidemic would be

one to three per 10,000 of the population. The risk of reaction is and must be gauged by the pediatrician and weighed carefully against the severity of the infection and the chance of taking the disease in a recognized or crippling form when the child is exposed to it.

Usefulness

The fact that an antigen is available to protect against a disease is not sufficient reason for its employment even though it be effective and reasonable in cost. An antigen against chickenpox or mumps would not likely receive enthusiastic acceptance from pediatricians because in children both diseases are generally mild and its probable value would be limited to weaklings or in the instance of mumps to protecting men against contracting the disease while in military service. It must be remembered that there are already a number of severe diseases for which antigenic agents are available and still others for which an agent would be highly desirable, and injections being what they are, mothers are not anxious to submit their infants and children to more "needles" unless they are convinced of exceptional benefit under the circumstances.

The risk of disease also is a factor in considering usefulness. Typhoid fever is a severe disease and an antigen has long been available for use, but the pediatrician in the northern part of the United States does not feel it necessary to inoculate his patients against typhoid fever because the incidence of the disease is so low that many thousands would have to be inoculated to prevent a single case. However, if parents wish protection for a child because they intend to travel where the hazard is greater, the pediatrician is willing to inoculate and may even suggest it on information that the family intends to travel in areas where the safety of milk and water is uncertain. Likewise, for children exposed to special risk with relation to any disease for which there is a satisfactory immunizing agent inoculation is suggested.

Ease of Administration

In general, the child to be inoculated, its parents, and the pediatrician are very grateful for an antigen which can be easily and quickly administered with a minimum of pain and discomfort to the recipient. The child to be inoculated must be reckoned with and

therefore the number of doses of antigen needed to complete a series of injections should be kept as low as possible. If the disease to be prevented is severe or the risk of infection great, a mother may raise no serious objections and will bring her child for subsequent visits, but she must be strongly convinced of an antigen's value to see her child undergo another distasteful and painful experience. However, the pediatrician does not wish to sacrifice effectiveness to the desirability of fewer doses and can usually convince the parents that additional doses are needed for more complete protection. There is at present great interest in the development of products for active immunization which contain multiple antigens. It would appear that two- and three-antigen preparations are now both effective and safe. Further development along this line will make the pediatrician's immunization schedule less cumbersome and more acceptable to patient and parent.

Cost

To the present, the cost of manufacturing biologicals has not been low for many reasons, of which not the least is the necessity of assuring a safe product. If the antigen is popular, mass production generally assures a product which is available to all of the pediatrician's patients. Cost is usually the least considered specification when the use of an antigen is contemplated for protection against a disease which is severe.

Summary

It is apparent from the foregoing discussion that the pediatrician looks upon the employment of an antigen from a very practical point of view. Even though he is dependent upon manufacturers to assure him of a quality product and upon field investigators to guide him in the indications for use, yet whether he utilizes the antigen or not will largely depend upon personal experience in his practice, tempered by certain specifications he employs.

THE PHARMACEUTICAL SURVEY— THE BEGINNINGS OF THE END*

By Edward C. Elliott, Director

Preliminary

SOMEWHAT more than two years ago I accepted a commission from the titular leaders to organize and to conduct an exploration of the region held or claimed by American pharmacy. This enterprise was put under way late in the Spring of 1946. Since then it has been my lot to have eight hundred days of *life with pharmacy*.

Here I am charged with the well-nigh impossible task of compressing an account of the happenings, observations, and conclusions of these many adventuresome days into the brief space of forty minutes. At the best, and even with the most of your generous indulgence, I can do no more than to present a partial account. If Lady Luck smiles upon me, I may be able to sharpen your interest in the first published records of the exploration.

The Pharmaceutical Survey

The base plan for The Pharmaceutical Survey was drawn by a group of the leaders of the profession five years ago. In all frankness, and with no apology, it should be stated that many of the things expected to be done by that plan have not been done; nor could some of these be done. The job proved to be much larger than originally conceived. Objectives that appeared near proved to be far away. Much had to be learned by the discouraging and time-consuming methods of trial and error. We have had to contend with the well-known perversity of inanimate things, as well as the prejudices and the procrastinations of human beings. Then, too, the matter of a certain quality of my own dumb-headedness must be held in mind.

Be it known that there is no intention of evading responsibility for what has not been done; nor for any apparent delay to bring the work of the Survey to its excepted completion.

---

* Presented at the American Pharmaceutical Association Convention, San Francisco, Calif., August 12, 1948.

Be it also known that the Survey could not have been carried on without the voluntary and sometimes the conscripted assistance of many hundreds of pharmacists and officers of pharmaceutical organizations who assisted in the gathering of essential facts. These facts were the much required raw material from which the Survey hoped to derive its results.

It is to be recorded in bold type that American pharmacy is permanently indebted to that group of fifteen pharmaceutical and lay leaders who make up the Committee on The Pharmaceutical Survey. Without their interest, wisdom and counsel, the Survey could not have gone forward.

The San Francisco Assignments

As you know, the masters of the programs assigned me for duty this week in three places. On Monday before the American Association of Colleges of Pharmacy, to present that portion of the Survey having to do with the program of education and training of those qualifying for admission to the profession of pharmacy; on Tuesday to discuss those matters affecting the State Boards of Pharmacy; and now here today, before the American Pharmaceutical Association, for an over-all viewing of the Survey. All the way from Washington to San Francisco I wondered about the temperature of these trials by fire.

First Purposes

Speaking before this Association in Pittsburgh two years ago, I said, "The broad, inclusive purpose of the Survey is to assemble, as far as may be possible with the means and resources available, those facts of education, of science, of business and of life that must be taken into account by those preparing men and women for the skillful performance of the duties belonging to those belonging to the profession of pharmacy." Throughout this has remained as the first business of the Survey.

The Old and the New Professions

At the Milwaukee meeting last year, it was said:

"There was an old profession of Pharmacy. There is coming to be a new profession of Pharmacy. The Pharmaceutical

Survey is primarily concerned with the characteristics, the standards, the practitioners and the problems of this new profession, the result of the continuing impact of modern scientific, educational, economic and other social forces.

Many of the elements of the old profession yet survive in the new. These tend to decline in number and utility. The new Pharmacy is taking on distinctive forms and functions. The primary questions to be answered by the Survey relate to these forms and functions. The answers, whatever these may be, may not fail to keep in mind that, while pharmacy will and must continue to realize its aspirations to be a truly scientific profession, pharmacy is ever practiced by and for individual human beings, individual institutions and individual communities."

To this may now be added, and emphasized, that the *end products of the Survey were to be programs of action designed and timed for the new profession of Pharmacy.*

General Plan of the Report

It is planned to publish the results of the Survey in three forms. In the plans for publication, these are referred to as (a) The White Book, (b) The Blue Book, and (c) The Gray Monographs.

The White Book, when completed, will be a document of approximately 100 pages. There will be summarized the principal findings and recommendations. It is hoped that it will be published in sufficient number to enable each and every member of the profession to have a copy. The steadily mounting costs of printing will be the determining factor.

The Blue Book will be a volume of approximately 400 pages. Here will be assembled the principal factual data regarding those phases of pharmacy with which the Survey has dealt.

The Gray Monographs will be a series of publications, each of which will treat with some selected phase of the Survey of particular interest to special groups. The first of these Gray Monographs already has been issued and deals with the predictive tests of students in the colleges and schools of pharmacy. The second Monograph will be ready for the printer shortly and will contain the results of the comprehensive analysis of more than 13,000 prescriptions.

The number of these Gray Monographs to be published will depend upon the availability of funds, conditions of publication, and distribution.

The White Book—First Draft

The first section of the White Book, presenting statements as to the origin, aims, and plans of the Survey, and containing ten groups of the first findings and approximately 60 specific recommendations for action, has been undergoing rigorous review by the Committee on The Pharmaceutical Survey. Final action will be had, it is confidently expected, at the meeting of the Committee to be held on September 26 and 27. Immediately thereafter this section will be published and distributed.

The White Book—Preview

While the Committee which, under the controlling plan of the Survey, is responsible for "developing or approving plans and policies for the Survey, for reviewing reports embodying the Survey data and for approving the conclusions and recommendations" has not taken final complete action, the Committee has issued to me the somewhat risky commission of presenting at this time to the American Pharmaceutical Association a preview of these first findings and recommendations. It may be that the Committee will change its mind about some of the matters between now and the end of September. In spite of this, it is proper that this Association be informed of the general trend of these findings and recommendations.

The Facts and the Committee

The first and oft-repeated instruction to the Director and the staff of the Survey was to get all of the critical facts, as far as available resources permitted, relating to present-day pharmaceutical education, practices, and services. This proved to be an endless undertaking. The more facts assembled, the more facts remained to be assembled. The real problem has been what to do with the facts when we had them. How often, after trapping facts as they were, we found ourselves in a trap. It was the old, old story of endeavoring to hold the bear by the tail.

It has ever been uppermost in mind that there is no inherent magic in facts. They must be tested, selected, related one with the other. Above all they must be translated into the terms of action;

action that does not overlook the prevailing and controlling ideas, habits, and agencies of the profession.

The committee in charge of the Survey has taken its job seriously. Its members have been openly determined to take whatever time was required completely to examine and carefully to weigh the facts before reaching conclusions. It has never been forgotten that the goal of the Survey was the preparation of programs of action for the production and promotion of the interests of pharmacy as a profession serving the health of the American peple. *Any approved recommendation for action must be workable from a practical point of view, and must be recognized as worth while from a professional point of view.*

The Findings and Recommendations

The White Book, in its present form, contains ten groups of Findings and Recommendations. These have to do with:

1. The supply of and the demand for trained pharmacists—professional manpower records.
2. The American Council on Pharmaceutical Education.
3. The teaching staffs of the colleges and schools of pharmacy.
4. Student selection, guidance, and testing.
5. State Boards of Pharmacy—Organization, financial support and functions.
6. State Boards of Pharmacy—Examinations for licensure.
7. State Boards of Pharmacy—Practical experience requirements for licensure.
8. The financing of pharmaceutical education.
9. The prescription study.
10. The pharmaceutical curriculum.

For each group there is presented a summary of the basic facts; the problem produced by these facts, or the absence of facts; and the resulting recommendations.

It was first hoped that the first section of the White Book would be printed and distributed for the San Francisco meeting. A combination of unforeseen and uncontrollable circumstances prevented this. In consequence it has been my responsibility to give, in summary form, some of the more important parts of the White Book.

Supply and Demand—Manpower Records

At the outset of the Survey it was evident that the facts of the present, essential for the planning of the future, were not available. As has been stated on numerous occasions, pharmacy has acquired neither the habit nor the skill of sound professional bookkeeping. This is notably the situation as to the supply of and demand for trained manpower for pharmacy. A sound manpower policy awaits the designing and construction of a firm foundation of country-wide statistical facts.

From this situation nine specific recommendations have resulted. The principal one of these proposes the setting up, under the auspices of the American Pharmaceutical Association, of a Commission on Professional Manpower. The Commission would be composed of one representative of each of the organizations holding membership in the National Drug Trade Conference, one representative of the Department of National Defense, and one representative of the U. S. Civil Service Commission. The chief functions of this commission will be to promote the development and maintenance of those basic records of the pharmaceutical profession, to assemble, coordinate, and publish each year those facts relative to the supply of and the demand for pharmacists for retail pharmacy, manufacturing and research establishments, teaching institutions, National Defense, state and national governments, and other fields of service.

A second recommendation proposes that pharmacy, pending the development of more reliable and purposeful data by the commission on pharmaceutical manpower, utilize an annual replacement factor of 3.1 for the projection of its manpower needs in place of the present factor of 2.6; and a third recommendation for the publication of a national roster of all pharmacists.

The remaining six recommendations of this group relate to the detailed application of the three major recommendations.

American Council on Pharmaceutical Education

There are nine recommendations relative to the American Pharmaceutical Association as the recognized national agency for the accrediting and betterment of colleges and schools of pharmacy. Chief in significance are the recommendations that the Council be provided with a full-time executive officer, *to be designated as Com-*

missioner for Pharmaceutical Education; that the Council have adequate support to enable it to exert needed constructive influences; and that there be adopted a system of classification of the accredited colleges of pharmacy.

In passing you may know that certain of the recommendations of the Survey, and a number of supplementary suggestions, have already been communicated to, and have been accepted by, the Council. It is firmly believed that the Council is destined to become a much more influential agency than it now is for the continuous advancement of pharmaceutical education.

Teaching Staffs

The Survey will present seven recommendations relative to the increase of the supply and the improvement of the quality of the members of the teaching staffs of the colleges and schools. These recommendations emphasize the importance of improving the standard of compensation for members of the teaching staffs. Special measures are proposed for the upgrading of members of existing staffs; for certain institutions to undertake programs of training for teachers; and for the American Foundation for Pharmaceutical Education to provide for teaching fellowships for the purpose of enabling individuals of ability and professional promise to become especially fitted for teaching service.

The factual evidence brought together by the Survey is conclusive that the future effectiveness of the colleges is directly dependent upon raising the levels of the scientific scholarship, of the teaching abilities, and of the compensation of the teaching staffs. This controlling element has been too long neglected by the profession.

Student Selection, Guidance and Testing

There are four recommendations designed to speed up the use of recognized intelligence and aptitude tests as factors for the selection and admission of students to the training institutions, and for the development of facilities for the continuance of guidance and counseling of students during the course of training. One of the recommendations would place upon each state and local pharmaceutical association the responsibility of engaging in the search for students of superior ability and to direct such students to the study

of pharmacy. The work of the Survey has confirmed the opinion held by many of those deeply concerned with the future professional status of the pharmacist that the need today is not for more students but for better students.

State Boards of Pharmacy

Inasmuch as the recommendations regarding the organization, financial support, functioning, examinations, etc., by state boards of pharmacy were discussed on Tuesday morning before the National Association of Boards of Pharmacy, this important section of the White Book might be passed over. In order that there is not a too wide gap in this record, mention should be made of the recommendations regarding the holding of a Convention for Pharmacy legislation for the preparation of a standard act to serve as a guide to the several states for their own pharmacy laws, to provide for more effective legal relationships of state and national agencies having to do with pharmacy; the organization, the financial support and functions of State Boards of Pharmacy, examinations for licensure and the so-called practical experience prerequisite.

The Financing of Pharmaceutical Education

The Findings and Recommendations regarding this critical matter are not yet complete. This much, however, is evident. The colleges of pharmacy, both the independent and state controlled, must receive larger support. The business of pharmacy is big business. By and large it is prosperous. The profession of pharmacy, on the other hand, is to be characterized as poverty-stricken. Yet the business cannot continue to progress and be prosperous without the profession. Ways and means must be devised whereby the profession of pharmacy directly benefits from the prosperity of the business of pharmacy.

Here I am speaking for myself, and not for the Committee on The Pharmaceutical Survey. Pharmaceutical industry and commerce are spending not less than three hundred million dollars each year for advertising and other means designed for the expansion of production and distribution. You may regard it as the wishful thinking of an old Hoosier school master for me to state that one per cent of this amount would not be an excessive allocation of

spending for the betterment of pharmacy as a profession. When I examine the data and observe the present low subsistence levels of the colleges and of the professional organizations of pharmacy, beginning with the American Pharmaceutical Association, I have misgivings for the future.

What new energy would be furnished the profession of pharmacy if the American Pharmaceutical Association and the state pharmaceutical associations had together not less than five hundred thousand dollars a year for their professional programs.

The Survey may not be able in all problem situations to tell pharmacy what to do. *The Survey can, with confidence, indicate what will happen in the event that nothing is done.* Take it as a bit of preaching or crusading, if you will. My twenty-seven months' experience working on the inside of pharmacy have convinced me that unless pharmacy provides for the support of professional things, just to the extent that such support is not provided will the realization of the aspirations of pharmacy be delayed and perhaps doomed. This is, I know, tough talk. It is intended to be tough, and tough with a smile of hope.

The Prescription Study

The results of the comprehensive analysis of 13,125 prescriptions collected in November 1946 from 220 pharmacists of 186 communities located in 39 states will be made available shortly in the form of one of the Gray Monographs. This study was designed primarily for the purpose of providing modern technical stuff for use in the training of students in pharmacy. It was not designed to be of direct assistance either to the manufacturers or to distributors. In this respect there may be certain disappointments. On the other hand, those concerned with the teaching of the modern science and practice of pharmacy will find in this study a wealth of new information. One is justified in stating that this study of prescriptions is far more fundamental than any other prescription study.

The Pharmaceutical Curriculum

In view of the presentation and discussion on Monday afternoon before the American Association of Colleges of Pharmacy, it is not necessary for me to indulge in any repetition. As you probably know, the major recommendation, indeed perhaps the major recommendation of all of those made by the Survey, has to

do with the lengthening and professionalization of the training of those who are to be *fully qualified* as professional pharmacists; those who will hold the degree of Doctor of Pharmacy and who will stand on a level of professional competency as do the members of other professions. This proposal, to be considered as radical by many, is intended to be a new horizon for the profession of pharmacy. To meet the existing situation, the Survey is proposing a considerable number of modifications of the so-called four-year curriculum now administered in most of the colleges. Especially important are those for the more effective instruction relating to the business aspects of retail pharmacy. A something more than a solvent business of pharmacy is required for the soundness of the profession of pharmacy. The good brains for pharmacy should also be brains for the good business of pharmacy.

The Things to Come

This small-scale, thumb-nail sketch of the first concrete outcomes of the Survey does not include certain other items which, in due course, will have their place in the first edition of the White Book. Those responsible for the Survey consider the matters already included to be of fundamental importance and entitled to positive action by pharmacy. Among the other matters yet to receive attention are:

1. The in-service training of pharmacists on the job.
2. The preparation of better textbooks for the students and teachers.
3. The definition of the relation of modern pharmacist and modern physician.
4. The place of women as pharmacists.
5. The organization of American pharmaceutical forces for action.
6. The many-sided problem of pharmaceutical economics.

Of these the last named has presented a long motley procession of stubborn facts. Like the mules of fiction and of reality, the economic facts look like strong, healthy animals, capable of pulling heavy loads. Only when one tries to put them in harness does the inward stubbornness become evident. And doubly so if one gets the harness on and attempts to get the load started. One is apt to

find himself off the road and in the ditch. Looking at the mule, one is tempted to be more profane than polite.

At the moment the processing of the considerable mass of information relative to retail pharmacy, especially that furnished by a group of nearly four hundred retail pharmacists, of all sections of the country, is being completed. The workable meaning of this information is yet to be determined. It may easily be that pharmacy will need to organize a *permanent Economic Commission* to consider and devise plans of action for solving the old and those new economic problems appearing day by day. There is an awareness on the part of the Survey that ways and means must be found for the practising, professionally-minded pharmacist to have an opportunity to secure an equitable return for his professional labors and upon his investment.

The crux of the matter is the adjustment of the ideals and needs of a free profession of pharmacy to the needs and ideals of a free enterprise economy. Frankly, the Survey does not know the answers to the multitude of questions that are presented. But the questions must be answered if pharmacy is to continue to be a profession. The situation, involving manufacturers, distributors and retailers of medicinals, and the medical profession is recognized as precarious and critical.

The Things of Shadow

Across the path of the Survey have appeared the shadows of things not included in the planned scope of the project. If the Survey were to be complete there would be included an analysis and forecasting of the influence upon the profession of pharmacy of the probable great expansion of American hospital facilities, of the establishment and operation of community and industrial health clinics, and of group medical services. Plans for the future of pharmacy may not omit these factors. They may require some creative, inspired guessing for the right actions.

The Beginnings of the End

The title appearing on the program was carefully selected—"The Beginnings of the End." You will recall that, as planned, The Pharmaceutical Survey was to continue in operation for three

years. Two years were to be utilized for the assembling and the interpreting of the data and the facts. The third year was to be given over to efforts to put the recommendations into effect.

It is worthy of note that in my experience of forty years with various educational and scientific enterprises known as surveys, this is the first time that definite provision was made to give reality to the results of a survey. In this the pharmaceutical leaders proved their wisdom. It now remains for the members of the pharmaceutical profession to provide proof that pharmacy is not a vanishing profession; but a vanquishing profession concentrating its strength to overcome those who would devaluate pharmacy as a health profession.

The defense rests. We expect your cross-examination.

SELECTED ABSTRACTS

Experimental Tuberculosis Treated With Sulphetrone. G. Brownlee and C. R. Kennedy. *Brit. J. Pharmacol. Chemotherapy 3:* 29 (1948). Forty guinea pigs were infected with 0.25 mg. of a 14-day old subculture of bovine tubercle bacilli. Twenty remained untreated and twenty were treated with an average of 0.6 Gm. of Sulphetrone (tetrasodium 1,1′-(sulfonylbis(*p*-phenyleneimino))-bis-(3-phenyl-1,3-propanedisulfonate) a day. The drug was given for the first fifteen days after infection. The average survival time of the non-treated group was 45 days while the treated group survived an average of 77 days. The bacilli were recovered in 19 of the treated animals.

Another group of guinea pigs received 0.25 mg. of a 21-day-old culture of human strain tubercle bacilli. Death resulted in 21 untreated animals within 154 days after the intramuscular administration of the culture material. On the other hand, only 6 of 24 similarly infected animals were dead within 154 days in the group treated with Sulphetrone. The extent and severity of the disease were much less in the treated animals. In a group of animals in which treatment was discontinued there was a resurgence of military tuberculosis.

The authors concluded that the drug is bacteriostatic but not capable of eliminating the organisms from the body.

Interrelations of Amino Acids and Vitamins. Editorial. *J. A. M. A. 137:*386 (1948). A number of recent experimental observations on the production of various deficiency states and their subsequent therapeutic control by varying the quantitative and qualitative dietary intake of amino acids and vitamins may have application to certain disease conditions in man.

An observation which suggests an interrelation between the amino acids and nicotinic acid showed that the amino acids trytophane and cystine exert some beneficial effects on human pellagra. Corneal

vascularization and ocular lesions in rats similar to those found in riboflavin deficiency were noted when the rats were fed a diet low in lysine, tryptophane or leucine.

Pyridoxine will prevent the inhibition of growth exerted on cultures of *Streptococcus lactis* by large amounts of glycine or serine in the medium as well as the toxic effects observed in animals given abnormal quantities of these amino acids. When protein depleted rats are fed a diet adequate in high quality protein but deficient in certain vitamins the replenishment of protein and the formation of antibodies is impaired.

It does not seem likely that the action of the amino acids is due to a direct replacement of vitamins but an adequate supply of the right types of amino acids seems to enable the animal or its intestinal flora of bacteria to synthesize the proper vitamins. On the other hand, the utilization of vitamins by the organism seems to be defective unless adequate amounts of the proper amino acids are available. Since dietary changes can bring about a marked change in the intestinal flora, and thereby in the quantitative and qualitative production of vitamins, control of the resultant manifestations of deficiency may be accomplished at times by controlling the intake of proteins.

Bousfield's Method for Reimmunization Against Diphtheria. P. Masucci, H. Gold, and R. J. DeFalco. *J. Pediatrics 32*:35 (1948). The authors administered varied doses of diphtheria toxoid in the form of compressed tablets to a group of 22 persons who had been immunized against diphtheria previously or who had at some time come in contact with the disease. They also administered the tablets to a second group of fifteen persons who were Schick-positive and who had no previous history of immunization or of exposure to the disease. Some of those in the first group received doses of four, others three, and still others two tablets each day for a period of seven days. The persons in the second group all received four tablets a day for seven days. The tablets were placed under the tongue and held there until they disintegrated completely.

The authors confirmed previous observation by Bousfield that diphtheria toxoid antigen can be absorbed effectively by the mucous membranes of the upper portion of the alimentary tract. In general,

there was a definite increase in the antitoxin titer in those individuals who had received previous diphtheria antigen or who had been exposed to the disease. A primary stimulus seems to be necessary in order to obtain a response from this type of immunization, for those in the second group showed no evidence of primary immunization. The amount of antigen absorbed is sufficient to act as a booster dose but will not produce primary immunization.

Although the authors feel that this method appears to be the most promising of non-parenteral methods of reimmunization thus far studied, the large dose of 2,1000 Lf units which is required may hinder its practical application.

Propylene Glycol as a Vehicle for Sulfathiazole in Otolaryngology. Roger W. Blackford. *Laryngoscope 58:*336 (1948). A 3 percent solution of sulfathiazole was dissolved in 100 per cent propylene glycol. The solution was used in one of three ways: the drainage wick inserted following incision was saturated with the solution, tampons saturated with the solution were placed on either side of the nose for 10 to 15 minutes following sinus operations, or 5 cc. of the solution were instilled into the maxillary sinus following irrigation.

As compared with 108 untreated control patients the 94 patients treated with the sulfathiazole solution generally recovered more rapidly. Those treated after otolaryngologic or oral surgery showed clearer postoperative fields. Those patients treated for nasal or auditory canal infections were quickly relieved of pain. No untoward reactions were noted in any of the patients.

This treatement was found to be ineffective in patients with chronic eczema of the external auditory canal, mycotic infections of the ear, or furunculosis of the external auditory canal.

The Administration of Penicillin for the Treatment of Gonorrhea by Means of the Hypospray. R. Hingson, E. Easley, A. Gray, C. Tucker, M. Kiesselbach, G. Parkhurst, G. Usher, and H. Davidson. *J. Ven. Dis. Inform. 29:*61 (1948). In the treatment of 206 gonorrhea patients the authors found that the administration of

penicillin by hypospray was just as effective as the administration of the antibiotic intramuscularly with a needle. Of the patients 93 per cent were Negro and 7 per cent were white. Also, 76 per cent were male and 24 per cent were female. There were 158 patients treated by hypospray of which 154 were cured while 48 were treated by needle injection and 47 were cured.

Each patient was given a total of 200,000 units of crystalline penicillin G. The doses were divided into 3 doses at one hour intervals of 50,000, 50,000, and 100,000 units, respectively. Procaine was added to the aqueous solution of penicillin for the needle injection and when added to the hypospray solution it was also found to reduce the pain. The last dose of 100,000 units of penicillin dissolved in 0.25 cc. of water for administration by hypospray caused intense local pain, erythema and edema lasting as long as 24 hours. Consequently, this last dose was given in two 50,000 unit doses dissolved in 0.25 cc. of water. No reaction other than a transient stinging sensation and a slight black and blue mark was then noted.

The authors found that the 125 lb. spring pressure of the hypospray which they used was not strong enough to penetrate the skin of some of the Negro male patients.

Para-Aminosalicylic Acid Found Helpful in Pulmonary Tuberculosis. A. Erdei and W. F. Snell. *Lancet 254:*791 (1948). Six cases of pulmonary tuberculosis are described by the authors, and the results of therapy with p-aminosalicylic acid. A daily oral dose of 12 Gm. was given but the authors feel that in further trials the dose should be increased to 20 Gm. a day. Therapy was continued for 60 days with 5 patients and 30 days with 1 patient. The only reason for discontinuance of therapy at this point was exhaustion of the supply of the drug.

Contrary to the findings of other clinicians no toxic manifestations were observed. Other workers most commonly reported gastrointestinal disturbances. The authors expressed the view that the toxic manifestations observed by others may have been due to impurities rather than to the PAS itself.

Following therapy with p-aminosalicylic acid there was a rapid reduction in the number of bacilli in the sputum. In addition the

clinical picture showed marked improvement with definite gains in weight. Two patients whose condition had deteriorated rapidly showed marked improvement following therapy with PAS with an improved sense of well-being, better appetite, and much less bacilli in the sputum.

PAS also seemed to have a direct antipyretic action. The drug is found in high concentration in the urine. This latter finding led to the postulation that it might have a beneficial influence on tuberculosis of the urinary tract.

The authors do not feel that p-aminosalicylic acid may be regarded as a cure for pulmonary tuberculosis but that its activity may cause it to be a valuable adjunct to present therapeutic measures.

Hydrogen Ion Concentration of Lachrymal Fluid. K. Pederson-Bjergaard. *Pharm. J. 160*:133 (1948). The hydrogen ion concentration of the lachrymal fluid has been rather commonly accepted as being about the same as that of the blood, expressed as a pH of 7.25 to 7.40. A few investigators have expressed a value somewhat higher. Most of the previous determinations have been made with indicator paper applied directly to the conjunctival sac.

The author collected 0.2 to 0.3 cc. samples of fluid from each of five normal men and five normal women. The pH was determined immediately by means of a colorimetric comparator paper and also electrometrically by means of glass electrodes. The pH varied from a low of 8.02 to a high of 8.45, colorimetrically, with an average of 8.24 and from a low of 8.0 to a high of 8.4, electrometrically, with an average of 8.22. Thus, the author pointed out that the lachrymal fluid has a higher pH than was generally assumed.

The author further pointed out that the eye can tolerate a 4.8 per cent solution of sodium sulfathiazole in water. The solution has a pH of 9.1, which is not high enough to cause irritation. This solution also happens to be isotonic with the tear fluid.

Pressor Effect of Desoxycorticosterone Acetate. M. L. Goldman and H. A. Schroeder. *Science 107*:272 (1948). Although the relationship of the adrenal cortex to arterial hypertension has been

a controversial one, there is evidence in some cases which suggests that adrenal cortex hyperfunction is concerned in the development of arterial hypertension.

In an effort to determine whether or not substances similar to adrenal cortex hormones have a direct vascular action, 5 mg. of desoxycorticosterone acetate was dissolved in 2.5 cc. of propylene glycol and injected intravenously. Five normal persons and five suffering with arterial hypertension were selected for the test. As a control 2.5 cc. of propylene glycol was injected into the same patients at different times.

The propylene glycol alone did not affect the blood pressure, but the injection of desoxycorticosterone acetate in the propylene glycol caused a prompt and significant rise in arterial pressure in those patients with arterial hypertension. There was no significant rise in the blood pressure of the normal individuals. In one hypertensive patient 5 mg. of progesterone was administered in the same fashion. A less marked rise in blood pressure occurred.

The responses which were obtained lasted for at least 30 minutes. Thus the authors concluded that desoxycorticosterone acetate acts as a pressor substance in hypertensive patients when injected intravenously.

Clinical Evaluation of Methadon. E. B. Troxil. *J. A. M. A. 136:*920 (1948). The analgesic drug, methadon, known also as 10820, has the chemical formula; 6-dimethylamino-4, 4-diphenyl-3-heptanone hydrochloride. A clinical evaluation of this drug in the production of analgesia in a total of 400 patients was reported by the author.

The drug was given orally as capsules, tablets, and elixir, and also hypodermically and intravenously. The action of the drug was evident within two minutes when given intravenously, within 15 to 20 minutes when given hypodermically or orally as the elixir, and within 30 minutes when given orally in capsules or tablets. The average duration of relief from pain was 3 to 4 hours by all routes of administration. It was found that 2.5 to 5 mg. doses relieved only very mild pain but that 7.5 to 10 mg. doses gave relief from intense pain.

The sedative effect from the drug was minimal as was the production of euphoria. A relaxing effect was also noted. Side effects were observed in 13 per cent of the patients and included nausea, vomiting, amnesia, dry mouth, pinpoint pupils, headache, and itching. Adequate or complete relief of pain occurred in 81 per cent of the 400 patients.

In comparison studies with morphine and meperidine hydrochloride it was found that 7.5 to 10 mg. doses of methadon were somewhat more effective than 10 and 15 mg. doses of morphine in the analgesia produced. With meperidine it was found that 10 mg. of methadon was equal in analgesic effect to 150 mg. of meperidine.

Methadon was found to be ineffective in the relief of labor pains. A development of tolerance was observed in a few patients. Addiction does not seem to develop since no signs of physical dependence nor withdrawal symptoms were observed.

BOOK REVIEWS

Basic Facts of Health Education. 193 pages incl. index. The Pharmaceutical Press, 17 Bloomsbury Square, London W. C. 1; 1948. Price 7s. 6d.

In 1943 the Pharmaceutical Society of Great Britain suggested to the British Ministry of Health that some means should be found for enabling pharmacists to obtain first hand knowledge on matters of general public health. As a result, articles were prepared by acknowleged experts and published at regular intervals in the *Pharmaceutical Journal.* This book represents a collection of such authoritative articles as published since 1944.

In reading through a number of these articles the reviewer was impressed with the clarity and the simplicity of their style; yet they were not lacking in scientific fact and information. A few of the subjects covered will give one an idea of the kind of articles that are included. Among the 52 topics are: Ante-Natal Care, Rickets, Food Poisoning, Cancer, Dysmenorrhea, Rheumatism, Athelete's Foot, Shingles, B. C. G. Vaccine, Venereal Disease and Geriatrics. Others of equal importance in the over all health picture are also covered.

Pharmacists, in particular, are in a strategic position to profoundly influence public health. It is an excellent idea to supply them with the kind of information that they can pass on to the public without transgressing their professional ethics. This book supplies just such information and it would indeed be as useful a book for American pharmacists as it must surely have proved itself for our English brothers.

L. F. TICE

Cosmetic Materials; Their Origin, Characteristics, Uses and Dermatological Action. By Ralph G. Harry. 479 pages. Leonard Hill Ltd., 17 Stratford Place, W. 1; London. Price: 35s. 0d.

This very useful book is essentially an encyclopedia of cosmetic materials both proprietary and non-proprietary. Each cosmetic

substance is described as to name or names, source, manufacture, physical and chemical properties, use and, finally, dermatological action. Much valuable data are presented that cannot readily be found except in widely scattered publications. The treatment given each substance as to its dermatologic effect is particularly useful. Not only is acute and chronic toxicity discussed but the likelihood of its being allergenic is carefully evaluated.

Not only will cosmeticians find the book of value but pharmacists and others who are interested in dermatological products, emulsions etc. The author seems to have done a careful job in compiling the data presented.

L. F. TICE

Chronica Botanica. Published by The Chronica Botanica Company, Waltham, Mass.; New York City—G. E. Stechert & Co.

"Luther Burbank, A Victim of Hero Worship." By Walter L. Howard, Ph. D. Price: $3.75. Volume 9, Number 5/6, 1946.

The book is very interesting because it reveals in 21 chapters (203 pages) the personality and the work of an "inventor" in the realm of plants, as it was with his friend, Thomas A. Edison, in the field of physics. Plate 17 shows him together with Edison and Henry Ford, now all dead. Just as the former, one of the greatest Americans, was not an educated physicist, so Burbank was not a trained botanist but a trained geneticist. Howard gives a very clear picture of a successful autodidact who became famous in the world with all his successes and disappointments and who lived at a time when very little was known about the laws of heredity and the function of hormones. The author describes also the man who stood behind this great work, and his fate.

"Goethe's Botany." By Agnes Arber, D. Sc. F. R. S. Price: $2.00. Volume 10, Number 2, 1946.

Goethe, the universal genius, was also interested in biology, and is famous for his discovery of the premaxillary bone in man. He also made great contributions to botany. The word "morphol-

ogy" was created by him, and he was the first to state that in dicots, also with alternate leaf position, the cotyledons are always opposite, always on the same node. Arber gives a historical introduction concerning Goethe's "Versuch die Metamorphose der Pflanzen zu erklaren." She then gives "A Note on Translations" followed by the English translation. Finally, accompanied by a "Prefatory Note," the original text in German is presented of the "Fragment," afterwards known as "Die Natur."

There are several illustrations in the book, and also original drawings of Goethe. Concerning Plate 26, showing the type specimen of the plant which is named for Goethe, *Goethea cauliflora,* the writer of this review takes the liberty to make some remarks. Underneath the reproduction, there may be read "Goethea cauliflora H. et M., type species of the genus Goethea, after jh. Wild's drawing in Nova Acta, vol. 2, pl. VIII.". On the sheet itself there is the note "Goethea cauliflora N. et M.", and as "Goethea cauliflora Nees" it is recorded in "Index Kewensis." The plant is a Malvaceae with red flowers, sitting on the stem; it is a native of Brazil. It was in honor of Goethe Gottfried Nees v. Esenbeck (1776-1858) and Carl Friedrich Philipp von Martius (1794-1868), Director of the Munich Botanical Garden, and collector of the plant in Brazil. The original type specimen which is reproduced in Arber's book is in the Martius Collection in the Herbarium of the Botanical Garden in Munich-Nymphenburg where most of the Martius' type specimens are deposited. (These were photographed a few years before World War II by the Field Museum in Chicago.) In 1932 it was loaned to the Goethe Anniversary Exhibition in Munich. During World War II the Martius Collection was not damaged; the Goethea-specimen is still in Munich.

"Merrilleana, A Selection from the General Writings of Elmer Drew Merrill, Sc. D., LL.D." Price: $4.00. Volume 10, Number 3/4, 1946.

Chronica Botanica is to be complimented on having published in a compendium of 260 pages the most important writings of Elmer Drew Merrill, one of the most successful botanists in this country. The scientist can obtain from this book a wealth of information which is often very difficult to find.

"The Arboretums and Botanical Gardens of North America." By Donald Wyman, Ph. D. Price: $1.50. Volume 10, Number 5/6, 1947.

This book presents a very good review about the botanical gardens in North America and Canada. The author also mentions the ownership, the personnel which is available, the size and the funds of the different gardens and the main field of their activities. There is an introductory chapter titled "How to establish an Arboretum or Botanical Garden," and then follows the description of the different gardens in the alphabetical sequence of the different States of this country and also the provinces of Canada.

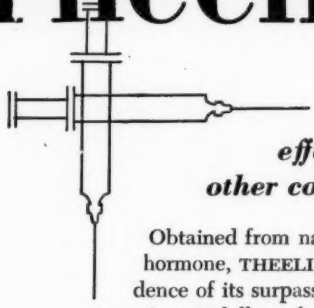
The book has illustrations of outdoor gardens and conservatories, and it contains maps as well. It includes a list of proposed arboretums and botanical gardens, and also a list of such institutions which have been discontinued. Finally, besides a "Bibliography" we find in the book a "small collection of special plants," a list of arborteums and botanical gardens where different plants are cultivated, as it is said in the book "given merely as a list of a few places where certain groups of plants can be observed in a large number of varieties."

T. P. Haas

dissolved IN OIL

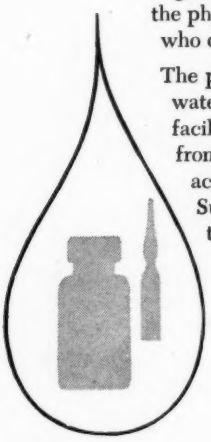
suspended IN WATER

Theelin



by intramuscular injection is highly effective in menopausal disturbances and other conditions requiring estrogenic therapy.

Obtained from natural sources, and standardized as the pure crystalline hormone, THEELIN during the past two decades, has given ample evidence of its surpassing excellence. Truly an estrogen of choice—THEELIN is gratefully welcomed by the patient who receives it, depended on by the physician who administers it, and highly regarded by the pharmacist who dispenses it.



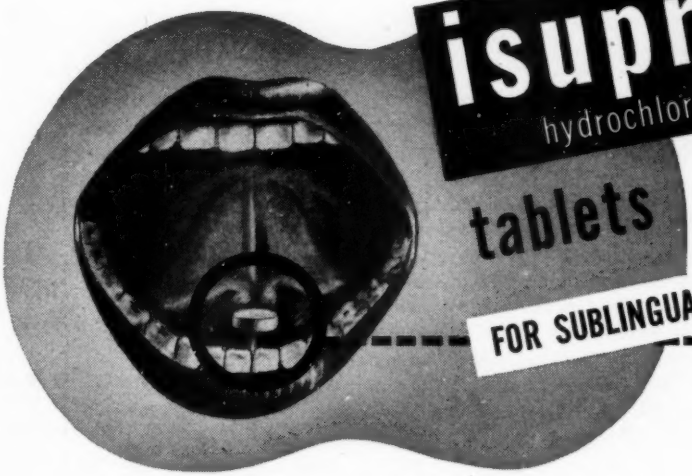
The physical properties of THEELIN—solubility in oil and insolubility in water—have been utilized to prepare forms of administration that facilitate versatile therapy. Thus, THEELIN in Oil is rapidly absorbed from the injection site, exerting its potent and well tolerated estrogenic action with efficiency and dispatch. Absorption of THEELIN Aqueous Suspension is slower and more sustained; the therapeutic effect is, therefore, produced over a more prolonged period of time. The particular form that is chosen depends on a number of factors, such as the intensity of symptoms, and the relative frequency with which the patient is seen by the physician.

Both THEELIN in Oil and THEELIN Aqueous Suspension are available not only in individual ampoules, but also in 10 cc. Steri-Vials® for greater economy. Whichever form is used, the patient is assured of effective relief of symptoms by a natural, pure, potent, crystalline estrogen.

PARKE, DAVIS & COMPANY · DETROIT 32, MICHIGAN

MEDICAMENTA VERA · PD CO.

NEW CONVENIENCE FOR ASTHMATICS
NEW PRESCRIPTIONS FOR YOU



isuprel®
hydrochloride
tablets
FOR SUBLINGUAL USE

For the prompt suppression of mild attacks of bronchial spasm, or as an adjunct to inhalation therapy in more severe cases, asthma sufferers now are offered the convenience of effective ISUPREL Sublingual Tablets.

This new potent bronchodilator—chemically: 1-(3′, 4′-dihydroxy-phenyl)-2-isopropylaminoethanol, is effective in many cases resistant to other treatment, and is characterized by a wide margin of safety.

For oral inhalation: 1:200 solution, bottles of 10 cc.
For sublingual use: 10 mg. tablets, bottles of 50.

WINTHROP-STEARNS

Winthrop-Stearns INC.
170 VARICK STREET, NEW YORK 13, N. Y.

CHECK your stock of . .

Theominal ®
Drisdol ®
Creamalin ®
Pluraxin ®
Neocurtasal ®
Neo-Synephrine ®
Deka ®
. . . Entire Winthrop-Stearns line on Fair Trade

As appearing in current Medical Journals

The Role of IODINE
in Clinical Diagnosis

• Diagnosis is the art or scientific process by which a disease is recognized. Success or failure in establishing a correct diagnosis depends in large measure on the use of reliable, safe and efficient clinical and laboratory procedures.

• Iodine compounds occupy a unique position as indispensable aids in providing X-ray evidence that is informative and most frequently complete. They supply the ideal contrast media for many diagnostic procedures — including bronchography, cholecystography, pyelography and myelography. Without these compounds, an accurate diagnosis might be difficult or impossible to make.

• Likewise in the fields of prevention and therapy, few medicaments serve such useful and varied purposes as Iodine with its many compounds and derivatives.

American Journal of Pharmacy

The American Journal of Pharmacy is the oldest continuously published scientific periodical of its kind in America, having been established by the Philadelphia College of Pharmacy in 1825. After the original issue there were three other preliminary numbers until 1829, when regular publication began. From then until 1852 four issues were published annually, with the single exception of 1847, when an additional number appeared. Six issues a year were printed from 1853 to 1870, at which time the Journal became a monthly publication.

Former Editors of the Journal have been: Daniel B. Smith, 1825-1828; Benjamin Ellis, 1829-1831; Robert E. Griffith, 1831-1836; Joseph Carson, 1836-1850; William Procter, Jr., 1850-1871; John M. Maisch, 1871-1893; Henry Trimble, 1893-1898; Henry Kraemer, 1898-1917; George M. Beringer, 1917-1921, and Ivor Griffith, 1921-1941.

Established and maintained as a record of the progress of pharmacy and the allied sciences, the Journal's contents and policies are governed by an Editor and a Committee on Publications elected by the members of the College.

Manuscripts should be sent to the Editor, who does not assume any responsibility in connection with the views or investigations of contributors of accepted manuscripts, other than to exercise general care in selection.

Contributors are allowed a reasonable number of copies of this Journal, free of charge, if applied for when the proof is returned.

Reprints, if desired, should be ordered when the proof is returned. The table below shows the *approximate* cost of reprints, the make-up of the pages to be identically the same as in the Journal. The actual cost may vary from the figures given, and will depend upon the amount of presswork, paper, binding, and other factors. Reprints containing half-tones may be expected to cost somewhat more than the rates given.

	2 pp.	4 pp.	8 pp.	16 pp.	Covers with Titles
50 copies	$3.50	$6.00	$10.50	$11.25	50 copies .....$ 5.00
100 "	4.25	7.00	14.00	15.00	100 " 6.50
250 "	5.25	9.00	18.75	20.00	250 " 10.25

Buy U.S. Savings Bonds
REGULARLY
Ask where you WORK
Ask where you BANK